

Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1, 2, 27-41, 43-47, 49, 50, and 52-96 are pending in the application, with 1 and 52 being the independent claims. Claims 3-26, 42, 48 and 51 are sought to be canceled without prejudice to or disclaimer of the subject matter therein. New claims 52-96 are sought to be added. Support for the amendment to claim 1 is found in the claims as originally filed. Support for the amendment to claim 31 is found in the specification at page 20, line 16. Support for the amendment to claim 41 is found in the specification at page 21, line 14 and page 89, line 25. Support for new claims 52-65 is found in the claims as originally filed and in the specification, *inter alia*, at page 5, lines 18-20. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Rejections under 35 U.S.C. § 112

Claims 1-45 have been rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. (Office Action, page 2). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that the claims are not enabled for the prevention of hyperproliferative disease. (Office Action, page 2).

Applicants respectfully disagree. Claims 3-26, 42, 48 and 51 have been canceled, rendering that portion of the rejection moot. Claim 1 as amended does not refer to the prevention of hyperproliferative diseases. Thus, the rejection has been rendered moot.

It is respectfully requested that the rejection of claims 1-45 under 35 U.S.C. § 112, first paragraph be withdrawn.

Rejections under 35 U.S.C. § 103

Claims 1-11 and 27-51 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Flack *et al.* (U.S. Patent No. 6,114,397) in view of Merck Manual of Diagnosis and Therapy. (Office Action, page 3). Applicants respectfully traverse this rejection.

The Examiner is of the opinion that:

'397 teaches a method and composition of employing gossypol, gossypol acetic acid, gossypolone and metabolites as effective in treating cancer (See for example the abstract and claims 1-14). '397 also teaches gossypol can be combined with other anti-cancer therapeutic agents such as cisplatin in a method and composition of treating cancer (see abstract and col. 2, line 65-col. 3, line 11).

'397 does not expressly teach the use of radiation in combination with gossypol compounds to treat cancer. '397 does not expressly teach the herein recited regimen of the compounds used such as route of administrations and the sequence of administration. '397 does not expressly teach the method of treating cancer employs the optical isomers gossypol compounds.

Merck Manual teaches that radiation is one of the common modalities in cancer treatment (See page 1276-1277).

It would have been obvious to one of ordinary skill in the art at the time of invention to employ both radiation and gossypol compounds of '397, as racemic or pure enantiomers, in a method and composition of treating cancer. It would have been obvious to one of ordinary skill in the art at the time of invention to optimize the therapeutic regimen of the cancer treatment employing the gossypol compounds and radiation.

One of ordinary skill in the art would have been motivated to employ both radiation and gossypol compounds of '397, as racemic or pure enantiomers, in a method and composition of treating cancer. Since both radiation and gossypol compounds of '397 are known to be useful in treating cancer individually, combining them in a composition or concomitantly employing them in a method of treating the very same disease (i.e., cancer) would be *prima facie* obvious, at least additive effect would be expected. '397 teaches a chiral center in the claimed compound, and illustrated separation for such optical isomers. It is well settled patent law that the skilled artisan, knowing a compound contains an asymmetric carbon atom, possesses all resultant optical isomers. The skilled artisan in possession of the designated compounds, possesses all isomeric forms of the compound for the old and well known antitumor utility. It is well known in the pharmaceutical art that various optical isomers will exhibit biological effects at various levels. Absent some difference in kind between the various isomers the skilled artisan would have seen each isomer as *prima facie* obvious (see *In re Adamson and Duffin*, 125 USPQ 233 (CCPA 1960)). The skilled artisan would have expected optical isomers to be separable and isomers so separated to exhibit physiological effects at varying levels. Possessing a compound known to contain chiral centers, places all the resultant compounds in the skilled artisan's possession. It would follow therefore, the instant claims recite *prima facie* obvious subject matter and are properly rejected under 35 USC 103.

One of ordinary skill in the art would have been motivated to optimize the therapeutic regimen of the cancer treatment

employing the gossypol compounds and radiation since optimization of the resulted parameters (e.g., dosage and regimen) is routinely done in the art and thus obvious as being within the purview of skilled artisan.

Examiner notes that the herein claimed mechanism of action of gossypol must be present in the method suggested by the cited prior arts since the products and its intrinsic properties cannot be separated.

(Office Action, pages 3-5).

Applicants respectfully disagree. Claims 3-26, 42, 48, and 51 have been canceled, rendering that portion of the rejection moot.

Claim 1 as amended is directed to methods of using specified gossypol compounds to treat or ameliorate hyperproliferative diseases. None of the specified gossypol compounds is disclosed in the '397 patent. Thus, one of ordinary skill in the art reading the '397 patent would not be motivated to use any of the claimed gossypol compounds in a method of treating hyperproliferative diseases. Furthermore, one of ordinary skill in the art would not have a reasonable expectation of success in using any gossypol compound that is not disclosed in the '397 patent in a method of treating hyperproliferative disorders as there is no teaching or suggestion in the '397 patent that all gossypol derivatives possess anti-proliferative activity or that any of the individually specified gossypol compounds in claim 1 possess anti-proliferative activity. The Merck Manual does not make up for the deficiencies of the '397 patent as the Merck Manual does not disclose methods of using any of the claimed gossypol compounds. Thus, there is no *prima facie* case of obviousness of claim 1 and dependent claims 27-41, 43-47, 49, and 50 over the cited art.

New claim 52 is directed to methods of treating or ameliorating hyperproliferative diseases comprising administering a gossypol compound and one or more second agent(s)

selected from docetaxel, paclitaxel, cisplatin, and/or radiation, wherein the combination of a gossypol compound and a second agent produces a synergistic effect with respect to one or more of tumor shrinkage, tumor loss, time to tumor progression, or survival. The '397 patent does not disclose any examples of combination treatment with gossypol and a second agent, and therefore does not show a synergistic response to combination treatment with respect to one or more of tumor shrinkage, tumor loss, time to tumor progression, or survival. One of ordinary skill in the art reading the '397 patent would not have a reasonable expectation that the particular claimed combinations of gossypol compounds with the specified anticancer agents or radiation produce a synergistic effect with respect to the specified outcomes. Thus, there can be no *prima facie* case of obviousness of claim 52 and dependent claims 53-95 over the cited art.

In contrast, the present specification discloses the synergistic effects of combinations of gossypol compounds with docetaxel, paclitaxel, cisplatin, and radiation in treating or ameliorating hyperproliferative diseases. See, *e.g.*, Examples 12, 16, 19, 20, and 22 and Tables 8-11, 14, and 15.

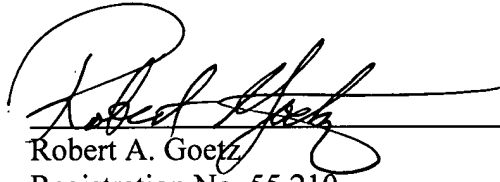
It is respectfully requested that the rejection of claims 1-11 and 27-51 under 35 U.S.C. § 103(a) be withdrawn.

Conclusion

All grounds of rejection of the Office Action of November 4, 2005 have been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that the claims should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicant encourages the Examiner to call the undersigned collect at (608) 218-6900.

Dated: _____

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